

Before discussing the Office Action, Applicant wishes to thank the Examiner in charge of the application for the courtesy of an interview on April 30, 1987, which has been very helpful in expediting decisions on the prosecution of the application. The possible submission of further evidence directed to other members of generic claim 15 has been considered by Applicant; and it was concluded that the compounds of the present Declaration are the only ones which are relevant to the question of obviousness. The Hamberger primary reference does not specifically disclose any compounds which are closer to the presently claimed compounds than the Hamberger example 16 and 17 compounds of the Declaration or which are sufficiently close for a comparison which would bear on the question of patentability. Applicant believes that the present Declaration makes the only meaningful comparisons that the Hamberger reference requires or would permit.

Applicant is enclosing with this Amendment a Request For Extension of Time of one month, which was required to consider possible additional showings and make a decision on how to proceed with the prosecution of this application.

The Examiner indicates that claims 9 and 19-22 and presumably claim 23 have been withdrawn from further consideration by the Examiner under 37 CFR 1.142(b) as being drawn to a non-elected species. It is assumed that upon allowance of generic claim 15, the withdrawn claims will be examined in accordance with MPEP 809.02 (a), (b), and (c).

Claims 3-5, 10-13, and 15-18 are rejected under 35

USC 103 over Hamberger et al in view of Martin et al and Berney (all of record). The Examiner indicates that Hamberger generically discloses compounds having the same basic structure as Applicant's compounds, which contain the same R₁, R₂, R₃, R₄, R₅ and R₆ substituents, and have the same utility as Applicant's compounds. The Examiner also indicates that Applicant's arguments and Declaration under Rule 132 submitted with the Amendment of September 29, 1986 have been considered but are not deemed to be persuasive of patentability. The Examiner argues that since the instantly claimed compounds are embraced by the broad claim of the Hamberger reference and have the same activity, the differences in activity shown in the Declaration is not considered significant. The Examiner notes that the mere fact that the Hamberger specification does not disclose an alkynyl substituted compound is not material in view of the equivalence suggested by the secondary art. The Examiner concludes that no invention is apparent over the teachings of the prior art which would suggest Applicant's compounds and their utility. Applicant respectfully disagrees and traverses the rejection.

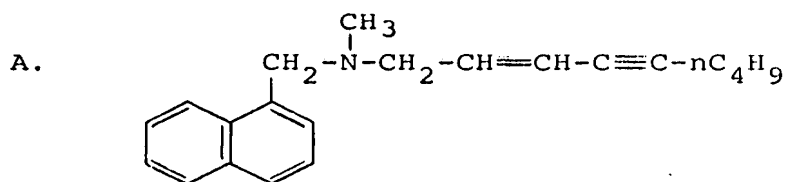
The only art relevant to the presently claimed subject matter is the Hamberger et al European Application No. 896. The secondary references are discussed below. As indicated by the Examiner, certain subject matter of the instant application in which substituent R₆ is a group of the formula IIIa can be constructed from the broad generic language of this reference. Hamberger does not disclose any compounds containing the IIIc group or which would suggest

this group, and these compounds are clearly patentable over the primary reference. Applicant's IIIa compounds can be obtained from the definition of the Hamberger R₆ substituent by selecting as R₆ a radical of formula IIIb (group v) in which g is 0 and R₁₄ is (C₃₋₁₂)-alkynyl. It is clear from the breadth of the reference, however, that this selection would only be made with direction from the instant application.

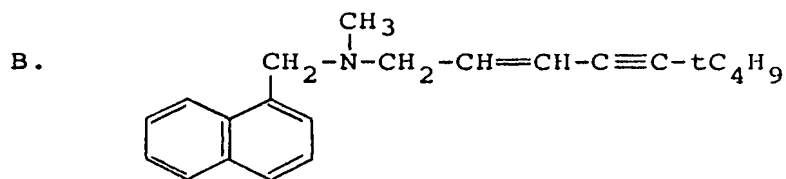
As noted in Applicant's September 29, 1986 Amendment, Hamberger does not clearly point to or exemplify any compounds which fall within the scope of the presently claimed invention. The reference indicates on page 6, lines 21-23, that the multiple bond is preferably at the remote terminal position of substituent R₆. In the present compounds, the alkynyl bond is in the -position of R₆, that is, in the position adjacent to the point of substitution. The teachings of Hamberger, therefore, in addition to not clearly pointing to Applicant's compounds would also lead away from them. It is only by picking and choosing from the broad language of the reference, guided by the teachings of the instant application, that one is able to construct the presently claimed compounds. There is no way that one skilled in the art using the Hamberger preferences and examples could take the reference and combine it with his own knowledge and be in possession of any of Applicant's compounds. Only with the instant application is one led to the compounds broadly embraced by Hamberger's terminology

and presently claimed. The Court of Customs and Patent Appeals indicated In re Taborsky (183 USPQ 50), that for obviousness, the prior art must provide one with motivation to make the molecular modifications needed to arrive at the claimed compounds. In the present case, Hamberger clearly does not provide that motivation; and accordingly, the instant compounds are patentable over the Hamberger et al reference.

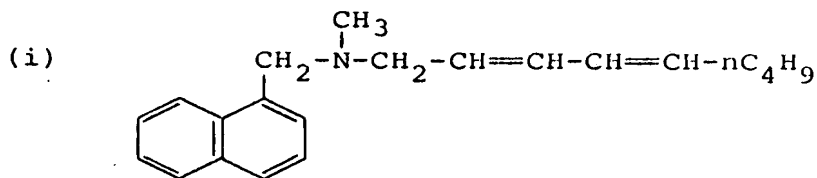
In support of the patentability of the instantly claimed compounds, Applicant submitted the Declaration under Rule 132 (37 CFR 1.132) referred to by the Examiner which compared the activity of Applicant's alkynyl derivative with the closest compounds specifically disclosed in the Hamberger reference, namely, the corresponding alkenyl derivatives. These are examples 3, (Claim 9), 16 (Claim 10) and 18 (Claim 23) from the present application and examples 16 and 17 from the Hamberger et al European Application No. 896. The compounds have the following structures:



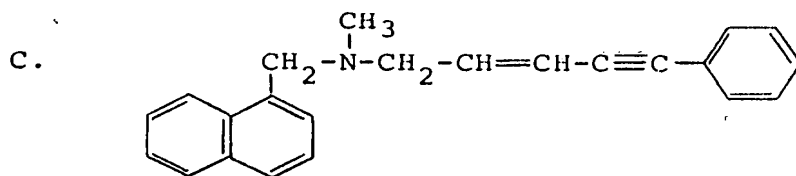
US Ser.No. 233,559
Example 3
Claim 9



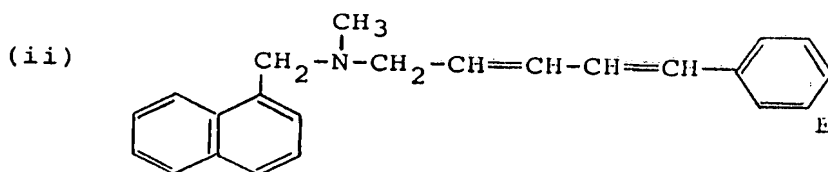
US Ser.No. 233,559
Example 16
Claim 10



EP Appln. No. 896
Example 17



US Ser.No. 233,559
Example 18
Claim 23



EP Appln. No. 896
Example 16

(All compounds in "trans" form)

The results in the Declaration show that Applicant's claim 9 compound A is approximately 2 to 8 times more active than reference compound (i) against the strains numbered 158, 150, 167, 177 and 39; and that the claim 10 compound B is approximately 4 to 60 times more active than (i) against all strains tested except *Candida albicans* 124. Applicant's claim 23 compound C is approximately 4 to 16 times more active than the closest Hamberger compound (ii) against strains 158, 150, and 167. The Examiner argues that the

difference in activity between Applicant's compounds and the reference compounds is not significant and that one skilled in the art would expect that the substitution of alkynyl for alkenyl would lead to compounds with a different degree of activity. Applicant, however, does not believe that it can reasonably be said that 2 to 8, 4 to 60 and 4 to 16 times greater activity is not significant and is a difference in degree not kind. Increases of these magnitudes are clearly completely unexpected especially in light of the preferences in the Hamberger reference. Applicant submits that the Declaration clearly rebuts any presumption of obviousness for the compounds of present claim 9, 10, and new claim 23, and that these compound are definitely patentable over the Hamberger et al reference.

With respect to remaining compounds in which R₆ is an alkynyl group, Applicant believes that the compounds of the showing are representative, and that the rebuttal of the presumption of obviousness also applies to the remaining alkynyl derivatives. These compounds are further removed from the closest compounds of the Hamberger reference, and there is no reason to believe that these compounds would have properties similar to the reference compounds rather than Applicant's compounds of claim 9, 10 and 23. The Declaration shows that it is the specific alignment of the alkynyl and alkenyl moieties in the instant compound that confers superiority, not the R₁ and R₆ substituents. The Examiner has cited no art which challenges this finding or Applicant's rebuttal of the presumption of obviousness. Applicant has clearly established that the claimed class of

compounds do, in fact, possess unobvious properties over the closest compounds of the prior art. Accordingly, the presently claimed invention is patentable over the prior art; and therefore, it is respectfully requested that the Examiner reconsider the instant rejection under 35 USC 103 and withdraw it.

With regard to the Martin et al and Berney secondary reference, the Examiner indicates that these references further set forth the equivalence of alkenyl and alkynyl substituents in amines and that the interchange of alkynyl for alkenyl would be expected to lead to compounds not necessarily with the same degree of activity but with the same properties. Applicant submits that the secondary references are not relevant. They in fact show that substitution of alkynyl for alkenyl completely changes not the degree of activity but the properties from anti-mycotic activity to mono-amine oxidase inhibition activity. These references would clearly lead one skilled in the art away from Applicant's compounds and their utility.

In view of the above amendments and comments, it is believed that the instant application is in condition for allowance; and accordingly, it is respectfully requested that the Examiner withdraw the rejection of the claims now in the application and pass the application to issue.

Respectfully submitted,

ANTON STUETZ

By Thomas O. McGovern
Thomas O. McGovern
Registration No. 25,741
(201) 386-8480

SANDOZ CORPORATION
59 Route 10
E. Hanover, N.J. 07936

Date: May 15, 1987

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Encls.: Request For Extension of Time (in duplicate)
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